UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,663	02/08/2002	Charles Larry Bisgaier	5730-C1-01-FJT	4182

28880 7590 08/11/2004

WARNER-LAMBERT COMPANY
2800 PLYMOUTH RD
ANN ARBOR, MI 48105

EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,663	BISGAIER ET AL.	
	Examiner	Art Unit	
	Shaojia A Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's amendment and response filed on May 4, 2004 wherein claims 31-33 have been amended. Claims 1-30 and 34-36 are cancelled previously.

Currently, claims 31-33 are pending in this application.

Claims 31-33 as amended now are examined on the merits herein.

Applicant's amendment filed May 4, 2004 with respect to the rejection of claim 33 made under 35 U.S.C. 112 second paragraph for the use of the indefinite recitation, i.e., " ACAT " of record stated in the Office Action dated November 4, 2003 have been fully considered and found persuasive to remove the rejection since the full name for "ACAT" has been recited in the claim. Therefore, the said rejection is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 31 as amended now is rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the particular compound of formula in claim 32-33 herein employed in a method for treating Alzheimer's disease, does not reasonably provide enablement for the employment any

acyl-coenzyme A: cholesterol acyltransferase (ACAT) inhibitors to be administered for the claimed methods of the particular treatments herein in a patient, for reasons of record stated in the Office Action dated November 4, 2003.

These recitation, "an acyl-coenzyme A: cholesterol acyltransferase inhibitor" or "an ACAT inhibitor", in claim 31, is seen to be merely functional language.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a method for treating Alzheimer's disease.

The relative skill of those in the art: The relative skill of those in the art is high.

The breadth of the claims: The instant claim 31 is deemed very broad since the claim reads on any ACAT inhibitor employed in the claimed method of treatment herein.

The amount of direction or guidance presented:

Functional language at the point of novelty, as herein employed by Applicants in claim 31, is admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC, 1997). The CAFC clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405(emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphases added).

In the instant case, "an ACAT inhibitor", recited in the instant claims is purely functional distinction. Hence, these functional recitations read on any compounds that might have the recited functions. However, the specification merely provides those particular compounds of formula for the claimed method of treatment herein (see page 6 of the specification).

Thus, Applicants functional language at the points of novelty in claim 31 fails to meet the requirements set forth under 35 U.S.C. 112, first paragraph, since it fails to provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (*General Electric Company v. Wabash Appliance Corporation et al.* 37 USPQ at 468 (US Supreme Court 1938)).

The predictability or unpredictability: the instant claimed invention is highly *unpredictable* as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art cannot fully described genus, visualize or recognize the identity of the members of the genus, by structure, formula, or chemical name, of the claimed subject matter, except those particular compounds of formula disclosed in the specification, as discussed above in *University of California v. Eli Lilly and Co.* Hence, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art would be unable to fully predict possible physiological activities of any compounds having claimed functional properties in the claimed method of treatment herein.

Moreover, one of skill in the art would recognize that it is highly unpredictable in regard to therapeutic effects for treatment of Alzheimer's disease in a human, side effects, and especially serious toxicity that may be generated by drug-drug interactions when and/or after administering any compounds represented by "an ACAT inhibitor" to a human, and/or while the patient also administering other medicines. See text book "Goodman & Gilman's The Pharmacological Basis of Therapeutics" regarding possible drug-drug interactions (9th ed, 1996) page 51 in particular. This book teaches that "The frequency of significant beneficial or adverse drug interactions is unknown" (see the

bottom of the left column of page 51) and that "Recognition of beneficial effects and recognition of and prevention of adverse drug interactions require a thorough knowledge of the intended and possible effects of drugs that are prescribed" and that "The most important adverse drug-drug interactions occur with drugs that have serious toxicity and a low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences" (see the right column of page 51) (emphases added).

In the instant case, in the absence of fully recognizing the identity of the members genus herein except those particular compounds of formula in the specification, one of skill in the art would not be able to fully predict the possible treatments herein and possible adverse effects occurring with many compounds having claimed functional properties to be administered to a human in the particular claimed method herein. Thus, the teachings of the "Goodman & Gilman's" book clearly support that the instant claimed invention is highly unpredictable.

The presence or absence of working examples and the quantity of experimentation necessary:

It is noted that the specification provides **no** working examples, i.e., testing results or data demonstrating that any ACAT inhibitors to be administered to a host e.g., a human,, or in vitro or vivo, are capable of treating Alzheimer's disease in a patient.

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the broad use of any compounds having those functions recited in the instant claims. As a result, necessitating one of skill to perform an exhaustive search for the

embodiments of any compounds having those functions recited in the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, the case *University of California v. Eli Lilly and Co.* (CAFC, 1997) and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test all compounds encompassed in the instant claims and their combinations to be administered to a host employed in the claimed methods of the particular treatments herein, with no assurance of success.

Response to Argument

Applicant's arguments filed May 4, 2004 with respect to this rejection made under 35 U.S.C. 112, first paragraph, for lack of full scope of enablement have been fully considered but are not deemed persuasive as further discussed below.

Applicant arguments that Applicants have provided support for the use of ACAT inhibitors in the methods of the present invention with the description of the hosts, dosages and modes of administration and the relevant assays and animal models for Alzheimer's disease with supporting data at page 9, line 27, to page 18, and that "Therefore, Applicants assert that they have provided enabling support for claim 31 of the present application", have been considered but not found convincing.

First, Applicants are reminded that this rejection is not made for lack of written description, but for lack of full scope of enablement of the broad use of any compounds represented by acyl-coenzyme A: cholesterol acyltransferase inhibitors or ACAT inhibitors in the claimed method.

As noted in MPEP 2111, during patent examination, claims are given their **broadest** reasonable interpretation. It is proper to use the specification to interpret what the applicant meant by a word or phrase recited in the claim, However, it is not proper to read limitations appearing in the specification into the claim when these limitations are not recited in the claim. See *In re Paulsen*, 30 F.3d 1475, 1480, 31 USPQ2d 1671, 1674 (Fed. Cir. 1994) for example.

In this case, the instant claims are **not** limited to those particular known ACAT inhibitors of Lee et al. (US 5,491,172) listed in the specification and CP113,818 (Pfizer) taught in Kovacs' Abstract, cited by Applicants in the remarks (at page 5 the last paragraph). Note that CP113,818 is the only one specific ACAT inhibitor that was mentioned and tested for reducing insoluble brain Aβ levels in a transgenic mouse model of Alzheimer's disease in Kovacs' Abstract.

Moreover, on the contrary to Applicants' argument that "they have provided enabling support for claim 31 of the present application", the instant claims read on administering to a patient any ACAT inhibitors. The recitation "an ACAT inhibitor" broadly encompasses those known and **unknown** compounds having the recited function as of the instant filing date. Note those **future known** compounds have not yet been discovered and/or made as of the instant filing date. Hence, those unknown or

future known compounds encompassed by claim 31 herein must required to additional or future research to discover, establish, make and/or verify their usefulness. Therefore, as indicated in the previous Office Action, the skilled artisan has to exercise **undue experimentation** to practice the instant invention.

Applicants argue that the courts have repeatedly made it clear that the PTO is not the Food and Drug Administration ("FDA"). Thus, Applicants assert that none of working examples is required. Applicants argument and assertion are not found convincing. As discussed above, in the absence of fully recognizing the identity of the members genus herein, the treatment of Alzheimer's disease in the claimed method is highly unpredictable.

The court indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute (see *In re Fisher*, supra). Lack of a working example is a critical and crucial factor to be considered, especially in a case involving an unpredictable and undeveloped art, i.e., the treatment of Alzheimer's disease. See MPEP 2164. The examiner agrees that PTO is not FDA, but patentability requires the satisfaction of the enablement statute. Thus, factual issues, i.e., working examples, are needed to comply with the enablement requirement of 112.

As pointed out in the previous Office Action, the specification provides **no factual data** in working examples, i.e., testing results or data demonstrating that any ACAT inhibitors to be administered to a host or in vitro or in vivo, are capable of treating Alzheimer's disease.

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the **broad use** of any compounds having the functions recited in the instant claims. As a result, necessitating one of skill to perform an exhaustive search for the embodiments of any compounds having the functions recited in the instant claims suitable to practice the claimed invention. Therefore, again, the skilled artisan has to exercise **undue experimentation** to practice the instant invention.

For the above stated reasons, said claims are properly rejected made under 35 U.S.C. 112, first paragraph, for lack of full scope of enablement.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 31-33 as amended now in Paper No. 8 filed on August 12, 2003 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (5,491,172, of record) in view of Scolnick (WO 95/06470, of record) for reasons of record stated in the Office Action dated November 4, 2003.

Lee et al. discloses that the instant compounds covered by the formula (I) in the patent lowers plasma-triglyceride and LDLC levels and increases HDL levels, and are useful for treating hypercholesterolemia and atherosclerosis by lowering the levels of

LDL cholesterol and elevating the levels of HDL in the serum. See abstract, col.1 lines 18-60, col.2, and claims 15-16.

Lee et al. does not expressly disclose that the instant claimed compound may be useful in a method of treating Alzheimer's disease.

Scolnick discloses that statins (HMG-CoA reductase inhibitors), which are known lower plasma-triglyceride and LDLC levels and increase HDL levels, are useful in methods of treating Alzheimer's disease. Moreover, Scolnick teaches that the reduction of cholesterol and plasma-triglyceride and LDLC levels may decrease risk of development of Alzheimer's disease and treat vascular related diseases such as Alzheimer's disease. See abstract, page 2 lines 16-20, page 10, and claims 1-25.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the instant compounds in methods of treating the onset of Alzheimer's disease herein.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the instant claimed compounds in methods of treating Alzheimer's disease since the instant compounds are known to be useful for lowering plasma-triglyceride and LDLC levels and treating hypercholesterolemia. It is also known that the reduction of plasma-triglyceride and LDLC levels may decrease risk of development of Alzheimer's disease and treat vascular related diseases such as Alzheimer's disease. Therefore, one of ordinary skill in the art would have reasonably expected that the instant compound would have beneficial therapeutic effects and

usefulness in the method of treating Alzheimer's disease by reducing or lowering plasma-triglyceride and LDLC levels in patients suffering therefrom.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Response to Argument

Applicant's arguments filed May 4, 2004 with respect to this rejection made under 35 U.S.C. 103(a) of record in the previous Office Action have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below.

Applicants argue that there is nothing in the cited prior art providing the motivation to substitute ACAT inhibitors in treating Alzheimer's disease taught in Scolnick since the mechanism of action of ACAT inhibitors herein differs from the prior art. Applicants' argument is not found convincing since both the particular ACAT inhibitor of Lee et al. and statins are capable of lowering plasma-triglyceride and LDLC levels. It is also known that the reduction of plasma-triglyceride and LDLC levels may decrease risk of development of Alzheimer's disease and treat vascular related diseases such as Alzheimer's disease. Therefore, one of ordinary skill in the art would have reasonably expected that the instant compound would have beneficial therapeutic effects and usefulness in the method of treating Alzheimer's disease by reducing or lowering plasma-triglyceride and LDLC levels in patients suffering therefrom.

Thus, motivation to combine the teachings of the prior art cited herein to make the present invention is seen. The claimed invention is clearly obvious in view of the prior art.

As discussed in the rejection under 35 U.S.C. 112, first paragraph, in the previous Office Action, the specification provides **no** working examples, i.e., testing results or data demonstrating that any ACAT inhibitors in vitro or in vivo for treating Alzheimer's disease in a patient. Note that arguments of counsel cannot take the place of factually supported objective evidence. See, e.g., In re Huang, 100 F.3d 135,139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); In re De Blauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984). Therefore, Applicants argument again that PTO is not FDA, is not persuasive.

Thus, Applicants are suggested to provide clear and convincing evidence of nonobviousness or unexpected results to rebut the prima facie obviousness rejection herein.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejection is adhered to.

In view of the rejections to the pending claims set forth above, no claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703.872.9307.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
August 4, 2004

SHAOJIA ANNA JIANG
PATENT EXAMINER